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60/415,929 **3 October 2002 (03.10.2002)** **US**
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(54) Title: **HUMAN PAPILLOMAVIRUS POLYPEPTIDES AND IMMUNOGENIC COMPOSITIONS**

(57) Abstract: The present invention provides immunogenic and pharmaceutical compositions for the treatment and prevention of human papillomavirus (HPV)-associated cancers and in particular, cervical cancer. In particular, this invention relates to fusion proteins, and the nucleic acids encoding these fusion proteins, used to generate immune responses against HPV. Specifically, this invention provides for fusions of HPV E6 and E7 in which the E6 and/or E7 contains one or more mutations. These mutations abrogate the transformation activity of these oncogenic proteins and, thus, confer safety to the E6/E7 fusions. In addition, these fusions maintain or increase the immunogenic efficacy of E6 and E7. Any gene or protein delivery method can be used to deliver or package the immunogenic compositions of the present invention.

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US03/31726

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 38/00; A61K 39/12

US CL : 530/300; 424/204.1

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 530/300; 424/204.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 6,004,557 A (EDWARDS et al) 21 December 1999 (21.12.1999), see the claims.	1-4, 11, 12, 16, and 21
Y	MANTOVANI et al. The Human Papillomavirus E6 protein and its contribution to malignant progression. Oncogene. 2001, Vol. 20, pages 7874-7887, see the abstract.	1-4, 11, 12, 16, and 21
Y	MUNGER et al. Biological activities and molecular targets of human papillomavirus E7 oncoprotein. Oncogene. 2001, Vol. 20, pages 7888-7898, see the abstract.	1-4, 11, 12, 16, and 21
Y	VELDERS et al. Eradication of Established Tumors by Vaccination with Venezuelan Equine Encephalitis Virus Replicon Particles Delivering Human Papillomavirus 16 E7 RNA. Cancer Research. 01 November 2001, pages 7861 to 7867, see Figure 3.	1-4, 11, 12, 16, and 21

☐ Further documents are listed in the continuation of Box C.☐ See patent family annex.

Special categories of cited documents:

- * "A" document defining the general state of the art which is not considered to be of particular relevance
- * "B" earlier application or patent published on or after the international filing date
- * "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- * "O" document referring to an oral disclosure, use, exhibition or other means
- * "P" document published prior to the international filing date but later than the priority date claimed

**

Later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

*X

document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

*Y

document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

*Z

document member of the same patent family

Date of the actual completion of the international search

Date of mailing of the international search report

03 November 2003 (03.11.2003)

05 JAN 2005

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BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-4, 11, 12, 16 and 21, drawn to human papillomavirus E6 and E7, and a method of inducing immune response. (1st product and method)

Group II, claim(s) 5-10, 13, 19, 20, drawn to isolated nucleic acid, expression vector and method of preventing cervical cancer. (2nd product and method)

Group III, claim(s) 14, and 15, drawn to a recombinant virus. (3rd product)

Group IV, claim(s) 17, and 18 drawn to methods of treating and preventing cervical cancer. (3rd method)

Group V, claim(s) 22, drawn to isolated polypeptide. (within the scope of SEQ ID NO: 3) (4th product)

Group VI, claim(s) 23, 25, drawn to isolated nucleic acid. (within the scope of SEQ ID NO: 3) (5th product)

Group VII, claim(s) 24, 26, drawn to isolated nucleic acid. (within the scope of SEQ ID NO: 4) (6th product)

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In order for more than one species to be examined, the appropriate additional examination fees must be paid. The species are as follows:

SEQ ID NO: 5, 9, 11, as they apply to Group V.

SEQ ID NO: 5, 9, 11, as they apply to Group VI.

SEQ ID NO: 6, 10, 12, as they apply to Group VII.

The inventions listed as Groups I-VII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The invention of Group I is known in the prior art as evidence by Edwards et al (US Patent No. 6,004,537) wherein the patent teaches the fusion protein of E6 and E7 human papillomavirus (see claim 1). The cited evidence proves that the technical feature of Group I does not make a contribution over the prior art. Thus, the claims are not so linked by a special technical feature within the meaning of PCT Rule 13.2.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: Each of the sequences listed confer different structure and presumably different effect.

INTERNATIONAL SEARCH REPORT

International application No.

US03/31726

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claim Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-4, 11, 12, 16 and 21

Remark on Protest ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

PCT/US03/0326

Continuation of B. FIELDS SEARCHED Item 3:
MEDLINE, BIOSIS, NPL, WEST, DERWENT, JPA, EPA
search terms: Papillomavirus, E7, E6, E7, immune response, mutant?